ANNEXES TO CHAPTER 3

Clinical Question IXb. Does the use of antiplatelet agents prior to arteriovenous fistula creation have an impact on patency and reduce the risk of thrombosis?

Three systematic reviews with meta-analysis were located, all published by the same group, which analysed the effects of anticoagulant therapy in patients with chronic renal failure (Palmer 2012; 2013 a; 2013 b).

No studies were found that compared giving only beforehand with give only afterwards, or giving before and after compared to only after.

As the studies found analyse perioperative treatment in all cases, i.e. before + after, the available evidence is considered to be indirect.

In patients having a fistula created for access

FISTULA - **Fistula failure (due to thrombosis or loss of patency)** The reviews provide information on five RCT in which the antithrombotic therapy begins before the operation to create a fistula as vascular access and continues for four or six weeks after, but there is a great deal of variation in the number of days prior to the operation in which the patients receive the drug in each study: Andrassy (1974) - one day before and then for 28 days; Fiskerstrand (1985) - starting 2 days before and for one month; Grontoft (1998) and Grontoft (1998) - start 7 days before and then for 28 days; Ghorbani (2009) - start 7 to 10 days before and then for 6 weeks. This meta-analysis also includes the study by Dember (2008) where they started on day 1 of the operation and then continued for 6 weeks. Antiplatelet therapy reduced the risk of thrombosis or patency failure by nearly half (6 tests, 218 events, 1365 participants, RR 0.54; 95% CI: 0.39 to 0.74; I^2=10%). **- Early access thrombosis (within 8 weeks) in fistulae** Antiplatelet therapy reduced the risk of early access thrombosis by nearly half (6 tests, 218 events, 1365 participants, RR 0.54; 95% CI: 0.39 to 0.74; I^2=10%). No significant differences were found between treatments in relation to: all-cause mortality, mortality from cardiovascular causes, fatal or non-fatal infarcts, fatal or non-fatal stroke, minor, major or fatal bleeding, primary loss of patency, need for intervention to maintain patency, or hospitalisation. **GRAFTS** In patients having access created by means of a graft, no differences were found between treatments for any of the outcome measures. - **Graft failure (due to thrombosis or loss of patency)** No significant differences were found between treatments (2 trials, 266 events, 756 participants, RR 0.94; 95% CI: 0.79 to 1.11; I^2=0%).	**Low quality**

Summary of evidence	
In patients having a fistula created for vascular access, thromboprophylaxis pre-surgery and lasting four to six weeks post-surgery reduces the risk of fistula failure (due to thrombosis or loss of patency) and is not accompanied by negative effects on other outcome measures.	**Low quality**
In patients having a fistula graft created for vascular access, thromboprophylaxis pre-surgery and for several weeks post-surgery shows no positive effect on any of the outcome measures.	**Low quality**
Patients' values and preferences *No relevant studies related to this aspect have been identified.*	
Use of resources and costs *No relevant studies related to this aspect have been identified.*	
Recommendations [Proposal]	
Weak	In patients having a fistula created for vascular access, we recommend thromboprophylaxis starting some days before and continuing for four to six weeks after to reduce the risk of access failure (due thrombosis or loss of patency).
Weak	In patients having a graft fistula created for vascular access, thromboprophylaxis is not recommended prior to the vascular access surgery.

References

Palmer SC, Di Micco L, Razavian M, Craig JC, Ravani P, Perkovic V, Tognoni G, Graziano G, Jardine M, Pellegrini F, Nicolucci A, Webster A, Strippoli GF. Antiplatelet therapy to prevent hemodialysis vascular access failure: systematic review and meta-analysis. Am J Kidney Dis. 2013 Jan; 61(1):112-22.

Palmer SC, Di Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, Jardine MJ, Webster AC, Zoungas S, Strippoli GF. Antiplatelet agents for chronic kidney disease. Cochrane Database Syst Rev. 2013 Feb 28; 2: CD008834. doi: 10.1002/14651858.CD008834.pub2.

Palmer SC, Di Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, Copetti M, Graziano G, Tognoni G, Jardine M, Webster A, Nicolucci A, Zoungas S, Strippoli GF. Effects of antiplatelet therapy on mortality and cardiovascular and bleeding outcomes in persons with chronic kidney disease: a systematic review and meta-analysis. Ann Intern Med. 2012 Mar 20; 156(6):445-59.

GRADE TABLES

Date: 2014-03-25
Question: Antithrombotic prophylaxis prior to the creation of the vascular access vs placebo?
Bibliography: Palmer SC, Di Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, Jardine MJ, Webster AC, Zoungas S, Strippoli GFM. Antiplatelet agents for chronic kidney disease. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD008834. DOI: 10.1002/14651858.CD008834.pub3.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antithrombotic prophylaxis	Placebo	Relative (95% CI)	Absolute		
Dialysis access failure (thrombosis or loss of patency)												
9	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	238/1094 (21.8%)	292/1043 (28%)	RR 0.66 (0.49 to 0.89)	95 fewer per 1000 (from 31 fewer to 143 fewer)	⨁⨁◯◯ LOW	CRITICAL
								25%		85 fewer per 1000 (from 28 fewer to 127 fewer)		
Dialysis access failure (thrombosis or loss of patency) - Fistula												
6	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	77/682 (11.3%)	141/683 (20.6%)	RR 0.54 (0.39 to 0.74)	95 fewer per 1000 (from 54 fewer to 126 fewer)	⨁⨁◯◯ LOW	CRITICAL
								21.5%		99 fewer per 1000 (from 56 fewer to 131 fewer)		
Dialysis access failure (thrombosis or loss of patency) - Shunt/graft												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	160/404 (39.6%)	149/352 (42.3%)	RR 0.94 (0.79 to 1.11)	25 fewer per 1000 (from 89 fewer to 47 more)	⨁⨁◯◯ LOW	CRITICAL

								42%		25 fewer per 1000 (from 88 fewer to 46 more)		
Dialysis access failure (thrombosis or loss of patency) - Fistula or graft												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	1/8 (12.5%)	2/8 (25%)	RR 0.5 (0.06 to 4.47)	125 fewer per 1000 (from 235 fewer to 867 more)	⨁◯◯◯ VERY LOW	CRITICAL
								25%		125 fewer per 1000 (from 235 fewer to 867 more)		
Early access thrombosis (before 8 weeks)												
6	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	77/682 (11.3%)	141/683 (20.6%)	RR 0.54 (0.39 to 0.74)	95 fewer per 1000 (from 54 fewer to 126 fewer)	⨁⨁◯◯ LOW	CRITICAL
								21.5%		99 fewer per 1000 (from 56 fewer to 131 fewer)		
Fatal or nonfatal myocardial infarction												
2	randomised trials	serious[1]	serious[4]	serious[2]	no serious imprecision	none	22/762 (2.9%)	25/764 (3.3%)	RR 0.82 (0.36 to 1.89)	6 fewer per 1000 (from 21 fewer to 29 more)	⨁◯◯◯ VERY LOW	CRITICAL
								3.6%		6 fewer per 1000 (from 23 fewer to 32 more)		
Fatal or nonfatal stroke												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	7/762 (0.9%)	4/764 (0.5%)	RR 1.77 (0.52 to 6.02)	4 more per 1000 (from 3 fewer to 26 more)	⨁⨁◯◯ LOW	

								0.6%		5 more per 1000 (from 3 fewer to 30 more)		
All-cause mortality												
7	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	140/1479 (9.5%)	166/1426 (11.6%)	RR 0.86 (0.71 to 1.04)	16 fewer per 1000 (from 34 fewer to 5 more)	⨁⨁⨁◯ LOW	CRITICAL
								8.2%		11 fewer per 1000 (from 24 fewer to 3 more)		
Cardiovascular mortality												
3	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	23/588 (3.9%)	35/591 (5.9%)	RR 0.67 (0.4 to 1.11)	20 fewer per 1000 (from 36 fewer to 7 more)	⨁⨁⨁◯ LOW	CRITICAL
								6.6%		22 fewer per 1000 (from 40 fewer to 7 more)		
Fatal bleeding												
4	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	2/816 (0.2%)	0/819 (0%)	RR 5.11 (0.25 to 106)	-	⨁◯◯◯ VERY LOW	CRITICAL
								0%		-		
Major bleeding												
6	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	12/1313 (0.9%)	14/1318 (1.1%)	RR 0.86 (0.4 to 1.84)	1 fewer per 1000 (from 6 fewer to 9 more)	⨁⨁⨁◯ LOW	CRITICAL
								0.3%		0 fewer per 1000 (from 2 fewer to 3 more)		
Minor bleeding												

4	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	6/513 (1.2%)	4/508 (0.8%)	RR 1.33 (0.25 to 7.14)	3 more per 1000 (from 6 fewer to 48 more)	⨁◯◯◯ VERY LOW	IMPORTANT
								2.1%		7 more per 1000 (from 16 fewer to 129 more)		
Loss of primary unassisted patency												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	258/329 (78.4%)	277/336 (82.4%)	RR 0.95 (0.89 to 1.03)	41 fewer per 1000 (from 91 fewer to 25 more)	⨁⨁◯◯ LOW	IMPORTANT
								60.5%		30 fewer per 1000 (from 67 fewer to 18 more)		
Failure to attain suitability for dialysis												
4	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	245/733 (33.4%)	239/726 (32.9%)	RR 0.66 (0.3 to 1.42)	112 fewer per 1000 (from 230 fewer to 138 more)	⨁⨁◯◯ MODERATE	CRITICAL
								29.8%		101 fewer per 1000 (from 209 fewer to 125 more)		
Need for intervention to attain patency or assist maturation												
3	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	101/764 (13.2%)	114/767 (14.9%)	RR 0.91 (0.72 to 1.14)	13 fewer per 1000 (from 42 fewer to 21 more)	⨁⨁◯◯ LOW	IMPORTANT
								12.5%		11 fewer per 1000 (from 35 fewer to 17 more)		
All-cause hospitalisation												

2	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	236/762 (31%)	248/764 (32.5%)	RR 0.96 (0.78 to 1.17)	13 fewer per 1000 (from 71 fewer to 55 more)	⨁⨁⨁◯ LOW	IMPORTANT
								34.9%		14 fewer per 1000 (from 77 fewer to 59 more)		
Cardiovascular hospitalisation												
2	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	195/762 (25.6%)	207/764 (27.1%)	RR 0.88 (0.58 to 1.33)	33 fewer per 1000 (from 114 fewer to 89 more)	⨁⨁⨁◯ LOW	IMPORTANT
								29.8%		36 fewer per 1000 (from 125 fewer to 98 more)		

[1] The authors of the Cochrane review point out the following limitations of the evidence from these studies : high or unclear bias risk in most trials included and details of few patients to analyse some effects, in particular the antiplatelet effects on the graft's function and the adaptation of the vascular access for the dialysis.

[2] The studies evaluated the intake of antithrombotic agents before and after the creation of the access, not the intake only before the creation of the access.

[3] Wide confidence interval at 95% .

[4] One study finds a protective effect and the other does not .